Product modification

Robert E Waller* and **Peter Froggatt†**

*Former *Scientific Secretary and †Chairman, Independent Scientific Committee on Smoking and Health, UK*

For more than 20 years there has been a coherent programme of product modification in the UK, involving the introduction of low tar brands of cigarettes and the gradual reduction in average tar yields over the whole range of manufactured cigarettes. The sales-weighted average tar yield has declined from 20.8 mg/cigarette in 1972 to 11.0 mg/cigarette in 1993. To some extent potential benefits to established smokers have been offset by their tendency to 'compensate' for reduced nicotine yields. Investigating such aspects has formed one part of a wide-ranging research programme to monitor effects of modified products on health. Collectively the studies show benefits in terms of smoke intake and health outcome related to reduced tar cigarettes, but the success achieved in reducing average tar yields and narrowing the range has limited opportunities to detect differential effects.

Following the findings in the early 1950s of the strong association between cigarette smoking and lung cancer[1–7], evidence soon accumulated linking smoking with other adverse effects[8]. Government and the health authorities, though quickly accepting the major findings[9], responded warily—and to many, inadequately—mainly through pressure on the industry to curtail its more extravagant marketing practices, through public awareness campaigns, and through advising smokers to stop and others not to start. The determinants and gradual development of policies have been described in detail elsewhere [10]. Despite these moves and accumulating medical evidence, total cigarette smoking, especially by women, rose inexorably[11] and by the early 1970s it was clear that more vigorous policies were required. These were increasingly focused on the toxicity of tobacco components and on product regulation, and a key move was to establish, in 1973, the Independent Scientific Committee on Smoking and Health (ISCSH) to advise Health Ministers and, where appropriate, the tobacco companies on the scientific aspects of matters concerning smoking and health[12]. Until its replacement (in 1994—see 'TPRT' below) the Committee has been at the centre of helping to formulate national smoking and health policies framed in the interests of the public health.

Its creation was timely. Throughout the 1950s and 1960s there were numerous developments in the US and Europe towards 'less harmful'

Address for correspondence: Mr Robert E Waller, Department of Health, Wellington House, 133–155 Waterloo Road, London SE1 8UG, UK

British Medical Bulletin 1996;**52** (No. 1):193–205

©The British Council 1996

2063632674

This article is for individual use only and may not be further reproduced or stored electronically without written permission from the copyright holder. Unauthorized reproduction may result in financial and other penalities. (c) ROYAL SOC MEDICINE PRESS LTD

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

cigarettes[13]. These involved tobacco technology—such as using some reconstituted tobacco sheet—but importantly also the introduction of filters, an outstanding marketing success driven by commercial rather than health considerations since (in the UK) excise duty was then levied on the tobacco content of cigarettes, enabling filter-tips to be sold more cheaply. Thus, between 1956 and 1970, consumption of cigarette tobacco declined by 9.6% but cigarettes sold increased by 28.5% by which time 4 in every 5 cigarettes were tipped[11]. Some, however, were designed to reduce 'tar', the particulate phase of cigarette smoke then held responsible for the carcinogenic activity[14]. These developments did not amount to a coherent, monitored policy, and it was the initial task of ISCSH to devise one. This required Government resolve and industry cooperation, clearly neither initially assured, and the determinants and developments of these have been fully described by one of us[10]. It is sufficient to say here that the programme designed by ISCSH, agreed by the tobacco industry, and negotiated by Government with the Tobacco Advisory Council (TAC) as part of a series of so-called 'voluntary agreements' in 1973, 1977, 1980 and 1984 is known as the 'product modification programme'. No country then, or since, has developed such a regulatory system, and it is described in detail in the ISCSH Fourth Report[12].

Tobacco 'substitutes' and 'additives'

The first step in the programme was a radical one: the feasibility and advantages of introducing synthetic tobacco substitutes to cigarettes to replace some of the natural tobacco. This required extensive testing of the toxicity of the substances themselves, in various mixtures with tobacco, and of the resultant smoke; and the formulation of testing guidelines for additives generally[15]. The original substitutes tested were 'New Smoking Material' (NSM) and Cytrel, each based on modified cellulose. They were submitted to ISCSH in 1973 but, because of the thoroughness of the test procedures, were not cleared for marketing until April 1977. On 1 July that year, 11 brands (and in a fortnight a twelfth) were launched each containing 25% 'substitute' and 75% natural tobacco. Consumer uptake was initially satisfactory but rapidly fell off for a variety of reasons; sales were soon negligible and the brands were withdrawn with much financial loss to the companies involved[16]. The invaluable toxicological testing expertise gained by the ISCSH was recognised by vesting the responsibility for approving all additives in the Committee, as part of the Voluntary Agreement of 1977, rather than in the Customs and Excise as previously, an authority which ISCSH has used judiciously but

2063632675

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

Table 1 Definition of tar bands

From 1972	Tar yield, mg/cigarette
Low	10 or less
Low to middle	11–16
Middle	17–22
Middle to high	23–28
High	29 or more*
From 1985	
Low	*under 10*
Low to middle	10 but less than 15
Middle	15 but less than 18
High	18 and above

*The highest quoted yield in 1972 was 38 mg. This band disappeared in 1980. The banding system was phased out during 1992, when actual yields of tar and nicotine were required to be printed on packets. From 31 December 1992, an absolute upper limit of 15 mg tar was imposed by regulation, and the limit is due to fall to 12 mg from 31 December 1997.

constructively as part of its later policies to make lower-yield cigarettes more acceptable to recalcitrant smokers.

Tar reduction

The failure of the 'substitutes' sounded a knell for radicalism in product modification; thereafter, the ISCSH and the tobacco industry were forced to a strategy of gradualism, reducing tobacco yields by such means as effective filters, increasing the porosity of cigarette papers, introducing ventilation holes near the tip of the cigarette, and ingenuities in tobacco chemistry and blending. Though aimed primarily at 'tar', they also reduced the yields of nicotine and of some gaseous components, though not necessarily *pro rata*[12], so that any harmful effects of non-tar components would also be reduced *pari passu*. Since July 1972, monitoring of (machine) yields of 'tar' and nicotine (and later of carbon monoxide) has been carried out by the Laboratory of the Government Chemist (LGC) through biannual surveys showing manufacturers' brands in rank order of tar yield within various tar-delimited 'bands' (Table 1), published by the Department of Health, over much of the time in leaflet and poster form for public information.

This policy of gradualism was based on two assumptions. First, that the important noxious materials—especially the carcinogenic ones—are in the tobacco tar and/or other products of combustion with a dose response relationship between the yields and smoking-related diseases without a significant threshold of safety. Evidence with respect to lung

2063632676

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

cancer at least favours this. In fact, since the programme also reduces nicotine and (some) gases, for it to be justifiable the noxa need not be in the 'tar' fraction. Second, that the programme is not such as to prompt significant 'consumer-resistance', i.e. through smoking more cigarettes; by switching to a stronger brand; or by 'over-smoking' a cigarette—longer and more frequent puffs, shorter butts, deeper pulls, etc., any of which would increase the smoker's tar exposure. The ISCSH consistently advised people not to smoke but could have little to say on commercial measures to combat the numbers of cigarettes smoked (e.g. advertising, tobacco tax) but it acted in two ways to reduce the toxicity of products available to smokers.

First, to encourage health-conscious but recalcitrant smokers, new products were introduced in the low tar band (<10 mg/cigarette) and smokers were encouraged by advice and selective advertising to switch to them: by February 1986, 33 of 138 brands in the LGC survey list were low tar as against only 13 of 121 in 1976[11]. This had an early, but later a less marked, success: the low tar brand market, less than 1% in 1974 rose steadily but plateaued around 15% in the 1980s. However, as yields of all products fall further to comply with new regulations, the market share in the low-tar range is tending to increase again.

Second, the yields of non-low-tar brands have been gradually lowered and the strong brand loyalty of most smokers has ensured very little switching to higher-yield brands. For monitoring, sales-weighted average tar yields (SWAT) were calculated across all tar bands pooled for each survey period using LGC data and industry figures for brand market share, with similar indices for nicotine and later carbon monoxide (Fig. 1).

Targets for SWAT were set in successive voluntary agreements based on proportionate rather than absolute reductions, and the 1980 Agreement specified a SWAT target of 15 mg/cigarette by the end of 1983—which was completely met—and of 'approximately' 13 mg/cigarette by the end of 1987[17]—which was nearly met. This policy was fortified by re-defining tar bands (Table 1), by restricting tar yields of new brands to 13 mg[17] and setting progressively reducing tar limits for existing brands[12]. This latter method has become the major thrust of product modifications in the 1990s as regulatory controls implementing EU Directives replace, in the UK, the voluntary agreements and bring the other EU countries under regulation based on this cornerstone of UK practice. Currently, there is an upper limit of brand tar yield of 15 mg/cigarette, set to become 12 mg by the end of 1997, though with some derogation for one member state. The UK is among the leaders with a SWAT now of only some 11 mg/cigarette (Fig. 1). In retrospect, the operational success of the product modification programme owes more to the gradual decrease in tar yields of popular mid-tar brands and consumer brand loyalty than to significant and deliberate switching by

2063632677

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

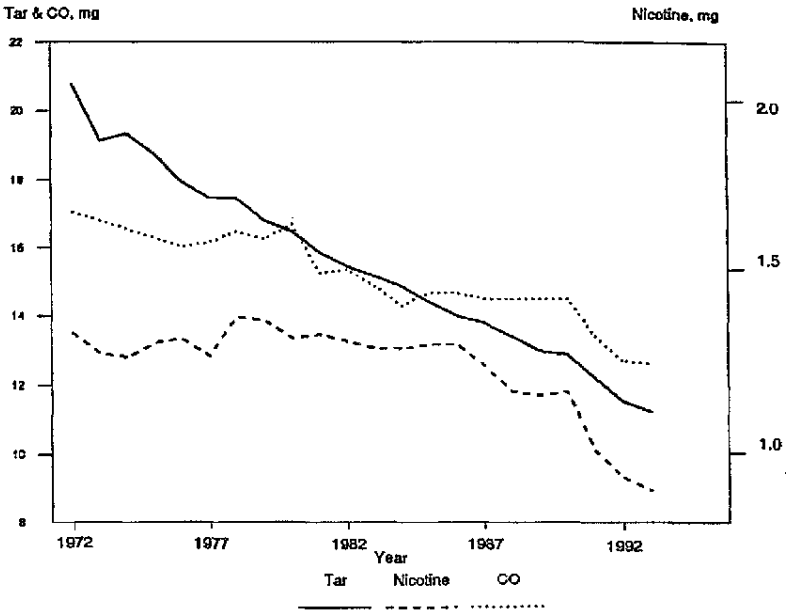

Fig. 1 Trends in sales-weighted-average yields of tar, nicotine and carbon monoxide from UK cigarettes since 1972, mg per cigarette. Calendar year averages based on a combination of data from the Laboratory of the Government Chemist, the Tobacco Manufacturers' Association and the ICRF Health Behaviour Unit.

smokers into low-tar brands. In consequence, the range of tar yields has contracted with brands, originally high-tar, having fallen most (Fig. 2). This is welcome to the public health but has had an inconvenient result: reduction in brand tar yield variance has made epidemiological studies of the effect of tar-yield on smoking-related diseases increasingly difficult as the ISCSH sponsored research proceeded (see 'TPRT' below).

Nicotine yields and 'compensatory smoking'

We have mentioned that the programme has depended *inter alia* on ensuring, as far as possible, that cigarettes with reduced yields are not 'over-smoked' otherwise uptake of 'tar' by the individual smoker could remain little changed, i.e. he (or she) will 'compensate' for the lower yields.

Such 'compensatory smoking' is motivated mainly, though not exclusively, by the need of individuals permanently or intermittently to restore their nicotine uptake per cigarette to their customary level without switching brands[18]. Until 1972, brand yields of nicotine decreased reasonably *pro rata* with tar, since steps to reduce one also reduced the other. Since then, commercial imperatives (retaining brand market share)

2063632678

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

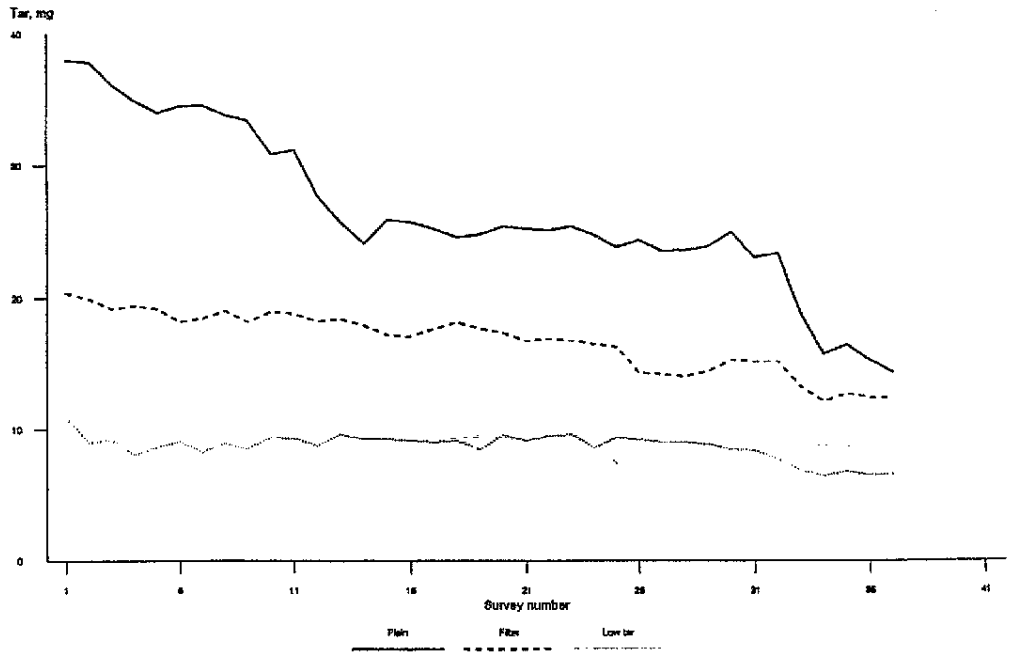

Fig. 2 Trends in tar yields for three representative brands of cigarettes monitored continuously from Survey 1 (July–December 1972) to Survey 37 (November 1993–April 1994).

have forced manufacturers to maintain nicotine yields as 'tar' has declined under the product modification programme. This was cautiously tolerated by the ISCSH who saw the use of consumer-optimum levels of nicotine (1.2–1.3 mg/cigarette in UK), which the evidence then suggested was not harmful to health, as a means of preserving brand loyalty as (harmful) tar was progressively reduced. Thus, between 1975 and 1987, sales-weighted average nicotine yields remained relatively unchanged while SWAT fell by 23%. Low nicotine brands, and the proportion of smokers smoking them, both increased—respectively from 23 to 37, and from 5% to 16%[11]. Clearly, there are technological limits to this approach and it also raises moral, philosophical, and political issues concerning using an habituating drug in this way, especially in the young and new smoker. It also supposes that nicotine in these doses is not harmful—a challenged assumption[19,20]. Nevertheless, ISCSH saw it as making a virtue out of a practical necessity, while also recommending future falls in sales-weighted average nicotine[12], which are now taking place. While a revised standard analytical method accounted for part of the decline around 1991, there is now a clear downward trend in nicotine yields, in line with the enforced reduction in tar yields (Fig. 1).

2063932679

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

This programme could be compromised by 'compensatory smoking'. The routine smoked-tobacco compounds' determinations are made on smoking machines using internationally agreed puff parameters[21] which, if varied, may change the absolute readings but not the rank order of brands for each component[12]. Nevertheless, the degree of 'compensation', i.e. individual uptake compared to machine-yield, is important. Biochemical markers in blood, urine or saliva, of which the nicotine metabolite cotinine is the most frequently used, can serve as measures of nicotine uptake, and proxies of uptake of other components and studies among smokers of different products[22] and of those switching from higher to lower yielding ones[23], generally show partial, but not complete, 'compensation'. To an extent 'compensation', therefore, reduces machine-yield-predicted advantages of lower-yielding products, but since under the programme tar yields have been allowed to fall appreciably more than nicotine yields, average tar uptake by individuals is still reduced. Furthermore, only exceptionally, if at all, could 'compensation' lead to uptakes even approaching machine-yields of 30 years ago (in 1965, SWAT was 31.5 mg/cigarette and SWAN 2.08 mg/cigarette[11]), so that the product modification has led to a significant reduction in 'tar' uptake per cigarette in nearly all smokers. More detailed information on the extent to which smokers compensate for reduced yields in modern cigarettes is now emerging from the TPRT research programme (see below).

Carbon monoxide and other smoke components

Carbon monoxide yields have been monitored routinely since 1976. The view of the ISCSH since its Third Report is that yields should be reduced on health grounds[17], but the reductions have not been as marked as those for tar (Fig. 1). Straightforward filtration has little effect on the gaseous components: only with ventilation techniques, as used in low-tar brands, are vapour-phase as well as particulate fractions reduced. This has meant that other gaseous components, possibly toxic, which would have been reduced *pari passu* with carbon monoxide, remain largely unchanged. This is undesirable since a basic empiric advantage of the product modification programme was that reductions in major and monitored particulate and gaseous phase components would be accompanied by reduction in other (recognised or unrecognised), possibly harmful, substances. A number of additional analytes which in higher concentrations in animals were known to be harmful were therefore studied. Brand yields from the LGC survey for October 1982–March 1983 were measured for total aldehydes, nitric oxide, hydrogen cyanide, acrolein

2063632680

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

and formaldehyde[12], and repeated for selected brands 3 years later[12], with phenols and PAHs subsequently added[24]. The mostly high positive inter-correlations[12] indicated justification for our empiricism and a policy of selective reduction was therefore not required. Nitric oxide was an exception but only in some continental and American brands which have relatively high nitrate contents[12,24].

Innovative products

In an effort to reduce the levels of harmful pyrolysis products and to produce less sidestream smoke, there have been developments of products that 'heat rather than burn tobacco'. One design, that has been the subject of extensive toxicological testing[25] comprises a carbon heat source, an aluminium capsule, spray-dried tobacco, glycerol, flavour, a tobacco-paper filter, a polypropylene filter and several sections of paper. Externally, the product is similar to a conventional cigarette and the smoker receives a glycerol-based aerosol carrying the nicotine and flavours from the tobacco, together with carbon monoxide and other vapour components. There have also been proposals to use electric heaters rather than carbon in such devices[26], but to date none of these products has been marketed successfully. Clearly such developments would radically change the concept of product modification and their impact in relation to public health would need careful scrutiny.

Product modification and smoking-related diseases

However valid the *a priori* case for the low-tar programme, its ultimate justification must depend on whether or not it contributes significantly to reducing the incidence of smoking-related diseases. We have argued that the programme's role in reducing lung cancer mortality, especially in younger age groups (who have not been exposed to high tar products in their shorter smoking history), has been established[12,27,28]. This is now supported by recent national data[29]. These show deaths from lung cancer now declining at all ages among men and under 65 years among women (Table 2), the trends being best interpretable as cohort effects with men born in the early 1900s—who reached smoking age at or after World War I, and women born in the 1920s—who reached smoking age at or after World War II, having the highest death rates. This decline in mortality has occurred more than expected on the basis of cigarette consumption alone, indicating that product modification has played a

2063632681

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

Table 2 Mortality rate per million in Britain from lung cancer by age, sex and calendar year

	Males										
	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84
1951–55	37	102	251	591	1244	2024	2564	2909	2568	2026	1413
1956–60	35	95	256	599	1262	2326	3368	3944	3861	3289	2221
1961–65	34	95	229	575	1241	2319	3716	4882	4974	4494	3367
1966–70	26	77	225	540	1170	2226	3719	5304	6213	5933	4525
1971–75	23	59	180	510	1081	2090	3554	5195	6825	7243	6058
1976–80	17	54	139	401	1009	1908	3346	4977	6692	7987	7638
1981–85	13	42	120	322	780	1731	3021	4574	6336	7753	8395
1986–90	8	34	104	276	600	1350	2691	4129	5850	7135	7975
1991–92	9	33	91	250	612	1135	2241	3936	5312	6542	7518
	Females										
	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84
1951–55	15	28	52	89	139	207	286	352	391	440	398
1956–60	15	31	63	105	171	243	331	387	454	496	459
1961–65	11	32	71	140	219	308	424	518	548	580	564
1966–70	11	31	82	164	286	401	512	653	729	740	671
1971–75	8	28	70	187	339	504	678	807	880	901	868
1976–80	7	27	65	164	374	583	869	1033	1112	1134	1060
1981–85	7	25	61	147	315	650	992	1313	1450	1462	1360
1986–90	6	21	63	141	276	583	1131	1496	1757	1769	1663
1991–92	4	17	62	147	289	499	1019	1608	1891	1976	1827

role in men under 60 beginning after 1965 and now emerging in young women[29].

A major problem in evaluating benefits of tar reduction in any more quantitative sense is that the risks of lung cancer in individuals are liable to be related to their whole histories of smoking, extending back to the high yielding products of much earlier decades, and yields of those smoked more recently provide little guide to overall exposures. There have, over the same period, also been favourable changes in some other factors of possible relevance to lung cancer risks, such as exposure to coal smoke. An increasing risk of lung cancer with both number of cigarettes smoked per day and tar yields has been reported from a prospective study in the US[30] and the authors considered that reductions in lung cancer risks were to be anticipated among smokers whose lifetime habits embraced only low-tar cigarettes. Support for this has come also from a case-control study[31] in which a significant trend in lung cancer risk in relation to tar yield was demonstrated.

Of the other 'smoking-related' diseases, of which the International Agency for Research on Cancer (IARC) lists some 30 within ICD numbers[32], the programme has probably been beneficial in chronic obstructive airway disease[27] but its role with respect to the others, including ischaemic heart disease, has not been unequivocally established.

2063632682

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

Future studies, including several on-going ones sponsored by the Tobacco Products Research Trust (see below), should elucidate some of these.

The product modification programme has also been beneficial in other ways: the reduction in the toxicity of cigarettes and the continued publication of their tar yields have reinforced the hazards of smoking, thereby encouraging some people to stop smoking as well as switching to lower tar brands, themselves less harmful and often a first step to complete cessation.

At the end of 1991, with the new regulatory controls on tar yields being introduced, the ISCSH was disbanded, to be followed by the establishment, in 1994, of the Scientific Committee on Tobacco and Health, with a wider remit.

The Tobacco Products Research Trust (TPRT)

The ISCSH early recognised that the auditing of the product modification programme must include research to assess its effect on the health of smokers. This would require a coherent, ISCSH-planned, research programme; eclectic research findings from the world literature would be inadequate. Under the Voluntary Agreements of 1980 and 1984 sums of up to £1m p.a. during 1981–1987 were made available by the tobacco industry through the Tobacco Advisory Council (TAC) for 'independent monitoring research into the effect on the health of smokers of modifications of tobacco products'. The ISCSH considered it advisable to establish a charitable Trust to administer these funds and the TPRT was registered with the Charity Commissioners in 1982. Applications were sought through advertisements in the medical and national press, and all grant and contract submissions were considered by ISCSH using referee systems and 'best practice', those approved being recommended to the Trust for funding. In this way an extensive programme of relevant research, latterly wider than direct epidemiological 'intervention' studies aimed to differentiate between effects of different types of products, which were operationally and technically difficult, was compiled. The Trust effectively terminated on 31 May 1995 with 36 projects completed, many large-scale fully funded, over 100 publications in scientific journals with others in preparation and over £8m committed. Three international symposia were also organised[18,33,34], the last two jointly with the Department of Health. It appears likely that the product modification programme will be further vindicated by the results of some of these studies, including new information in relation to ischaemic heart disease[35]. The latter study also investigated the effect of compensatory

2063632683

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

smoking on the uptake of smoke components by smokers of products in different tar bands, reporting that the mean plasma cotinine level was 19% higher in the medium-tar as compared with the low-tar group, not as great a difference as the 52% difference in mean yields of nicotine, but still representing a helpful reduction in uptake for low-tar products.

Detailed analyses of the uptake of both nicotine and carbon monoxide have also been reported recently from the 'tar reduction study' carried out under the TPRT programme[36]. Overall compensation for carbon monoxide was 65.4% and for nicotine 78.8%, the lower value for carbon monoxide reflecting the fact that the proportionate reduction in the yield of low tar to high tar cigarettes is greater for carbon monoxide than for nicotine. A full description of the Trust and its sponsored research will be published shortly[37]: some of the earlier studies have already been reviewed[12].

Conclusion

Since the early 1970s, product modification has formed part of the overall strategy to reduce the impact of smoking on public health. There has been a substantial reduction in the prevalence of smoking among adults, resulting from cessation activities[38] and trends in a number of smoking-related diseases are becoming more favourable[29]. The specific role of product modification is difficult to separate from that of changes in prevalence, but much evidence has accumulated to show that smoke intake has been reduced, and consequent reductions in adverse effects are to be anticipated. The prime message must at all times be not to smoke, but for the dependent adult smoker who fails to heed such advice there is no longer any access to strong high-yielding products, and, with current policies forcing tar yields and effectively nicotine yields down even further there is the prospect too that young people who may still experiment with smoking at an early age will be less likely to become addicted and to continue the habit. Providing that governments or smokers do not come to regard reductions in tar yields as substitutes for the avoidance of cigarettes, the further reduction, to 12 mg/cigarette in the regulatory upper limit, will help to reduce the number of premature deaths from tobacco[35].

Acknowledgements

The views expressed in this article are the personal views of the authors and they do not necessarily reflect those of other members of the former

2063632684

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

Independent Scientific Committee on Smoking and Health, or of the Department of Health, or of other organisations referred to.

All the analytical work referred to here was undertaken by the Laboratory of the Government Chemist (LGC) and we would like to thank Geoffrey Phillips and Keith Darrall in particular for supplying data. The Tobacco Manufacturers' Association provided information on sales-weighted averages, based on LGC analyses, and we would also like to thank Martin Jarvis of the ICRF Health Behaviour Unit for further contributions on this topic. The product modification programme owes much of its success to the guidance provided by members of the Independent Scientific Committee on Smoking and Health and we are indebted to the Trustees of the Tobacco Products Research Trust and to the Scientific Liaison Officer, Cheryl Swann, for their contributions on research aspects.

References

1 Schrek R, Baker A, Ballard GP, Dolgoff S. Tobacco smoking as an etiologic factor in disease. 1. Cancer. *Cancer Res* 1950; 10: 49–58

2 Mills CA, Porter MM. Tobacco smoking habits and cancer of the mouth and respiratory system. *Cancer Res* 1950; 10: 539–42

3 Levin ML, Goldstein H, Gerhardt PR. Cancer and tobacco smoking. *JAMA* 1950; 143: 336–8

4 Wynder EL, Graham EA. Tobacco smoking as a possible etiologic factor in bronchogenic carcinoma. A study of six hundred and eighty four proved cases. *JAMA* 1950; 143: 329–36

5 Doll R, Hill AB. Smoking and carcinoma of the lung: preliminary report. *BMJ* 1950; 2: 739–48

6 McConnell RR, Gordon KCT, Jones T. Occupational and personal factors in the aetiology of carcinoma of the lung. *Lancet* 1952; 2: 651–6

7 Doll R, Hill AB. A study of the aetiology of cancer of the lung. *BMJ* 1952; 2: 1271–86

8 Royal College of Physicians of London. *Smoking and Health*. London: Pitman Medical, 1962

9 Hansard HC, 1953–4, vol 523, col 173-4W

10 Froggatt P. Determinants of policy on smoking and health. *Int J Epidemiol* 1989; 18: 1–9.

11 Wald N, Kiryluk S, Darby S, Doll R, Pike M, Peto R. eds. *UK Smoking Statistics*. Oxford: Oxford University Press, 1988

12 Independent Scientific Committee on Smoking and Health. Fourth Report. London: HMSO, 1988

13 National Cancer Institute. *Toward a less harmful cigarette*. Monograph 28. Bethesda MD: National Cancer Institute, 1968

14 Wynder EL, Hoffmann D. *Tobacco and Tobacco Smoke*. New York: Academic Press, 1967

15 Independent Scientific Committee on Smoking and Health. First report. London: HMSO: 1975

16 Van Rossum R. The great substitute disaster. *The Grocer*; 16 September 1978

17 Independent Scientific Committee on Smoking and Health. Third Report. London: HMSO: 1983

18 Wald N, Froggatt P. eds. *Nicotine, Smoking and the Low Tar Programme*. Oxford: Oxford University Press, 1989: Section III, pp 85–236

19 Hoffmann D. Nicotine, a tobacco-specific precursor for carcinogenesis. In: Wald N, Froggatt P. eds. *Nicotine, Smoking and the Low Tar Programme*. Oxford: Oxford University Press 1989: pp 24–40

20 Editorial. Nicotine use after the year 2000. *Lancet* 1991; 337: 1191–2

2063632685

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000

21 Johnson JC. The development of machine smoking parameters for the measurement of cigarette tar yield in the United Kingdom. *J Assoc Off Anal Chem* 1986; 69: 598–600

22 Wald NJ, Boreham J, Bailey A. Relative intakes of tar, nicotine and carbon monoxide from cigarettes of different yields. *Thorax* 1984; 39: 361–4

23 Benowitz NL, Jacob P. Nicotine and carbon monoxide intake from high and low yield cigarettes. *Clin Pharmacol Ther* 1984; 36: 265–9

24 Phillips GF, Waller RE. Yields of tar and other smoke components from UK cigarettes. *Food Chem Toxicol* 1991; 29: 469–74

25 RJ Reynolds Tobacco Company. *Chemical and biological studies on new cigarette prototypes that heat instead of burn tobacco.* Winston-Salem NC: RJ Reynolds Tobacco Company, 1988

26 Davis RM, Slade J. Back to the future—with electrically powered cigarettes. *Tobacco Control* 1993; 2: 11–12

27 Darby SC, Doll R, Stratton IM. Trends in mortality from smoking related diseases in England and Wales. In: Wald N, Froggatt P. eds. *Nicotine, Smoking and the Low Tar Programme.* Oxford: Oxford University Press, 1989: pp 70–82

28 Froggatt P, Wald N. The role of nicotine in the tar reduction programme. In: Wald N, Froggatt P. eds. *Nicotine, Smoking and the Low Tar Programme.* Oxford: Oxford University Press, 1989: pp 229–35

29 Doll R, Darby S, Whitley E. Trends in smoking related diseases. In: Charlton J, Murphy M. eds. *The Health of Adult Britain, 1841–1991.* Decennial Supplement, Office of Population Censuses and Surveys. London: HM Stationery Office, 1995: In press

30 Stellman SD, Garfinkel L. Lung cancer risk is proportional to cigarette yield: evidence from a prospective study. *Prev Med* 1989; 18: 518–25

31 Kaufman DIV, Palmer JC, Rosenberg L, Stolley P, Warshauer E, Shapiro S. Tar content of cigarettes in relation to lung cancer. *Am J Epidemiol* 1989; 129: 703–11

32 International Agency for Research on Cancer. *Tobacco smoking.* Monograph 38. Lyon: IARC, 1986

33 Wald N, Baron J. *Smoking and Hormone-Related Disorders.* Oxford: Oxford University Press, 1990

34 Poswillo D, Alberman E. *Effects of Smoking on the Fetus, Neonate and Child.* Oxford: Oxford University Press, 1992

35 Parish S, Collins R, Peto R *et al.* Cigarette tar yield and non-fatal myocardial infarction: 14,000 UK cases and 32,000 controls. *BMJ* 1995; 311: 471–7

36 Frost C, Fullerton FM, Stephen AM *et al.* The tar reduction study. Randomised trial of the effect of cigarette tar yield reduction on compensatory smoking. In press

37 Swann C, Froggatt P. The Research Programme of the Tobacco Products Research Trust, 1982–1995. In press

38 Department of Health. *Smoke-free for Health.* London: Department of Health, 1994

2063632686

Source: https://www.industrydocuments.ucsf.edu/docs/kgdl0000